

1 Claims

2

3 1. A method of inducing and/or enhancing
4 expression of one or more of the genes of cells
5 of a biological sample,
6 said genes being the genes encoding one or more
7 of Raf, K-ras, SLAP, phosphoinositide 3-kinase,
8 COP9 homolog (HCOP9), apoptosis specific
9 protein, APO-1 cell surface antigen, FLIP
10 protein, cyclin G, CDC2 , cyclin-dependent
11 protein kinase -2, thymosin β -10, myosin light
12 chain (MLC-2), gelsolin, thymosin β -4, SSAT,
13 spermidine synthase, spermidine
14 aminopropyltransferase, MAT-8 protein, annexin
15 II, annexin IV, FGF receptor 2, transmembrane 4
16 superfamily protein , chaperonin 10, enoyl-CoA
17 hydratase, nicotinamide nucleotide
18 transhydrogenase, ribosomal protein S28,
19 ribosomal protein L37, L23 mRNA for putative
20 ribosomal protein, and/or ribosomal protein L7;
21 said method comprising administration of a
22 chemotherapeutic agent to said sample.

23

24 2. A method for evaluating in vitro the response
25 of tumour cells from a subject to the presence
26 of a chemotherapeutic agent to predict response
27 of the tumour cells in vivo to treatment with
28 the chemotherapeutic agent, which method
29 comprises:
30 (a) providing an in vitro sample from a subject
31 containing tumour cells;
32 (b) exposing a portion of said sample of tumour

1 cells to said chemotherapeutic agent;

2 (c) comparing expression of one or more of the

3 genes encoding Raf, K-ras, SLAP,

4 phosphoinositide 3-kinase, COP9 homolog

5 (HCOP9), apoptosis specific protein, APO-1 cell

6 surface antigen, FLIP protein, cyclin G, CDC2 ,

7 cyclin-dependent protein kinase -2, thymosin β -

8 10, myosin light chain (MLC-2); gelsolin,

9 thymosin β -4, SSAT, spermidine synthase,

10 spermidine aminopropyltransferase, MAT-8

11 protein, annexin II, annexin IV, FGF receptor

12 2, transmembrane 4 superfamily protein ,

13 chaperonin 10, enoyl-CoA hydratase,

14 nicotinamide nucleotide transhydrogenase,

15 ribosomal protein S28, ribosomal protein L37,

16 and/or ribosomal protein L7 and/or L23 mRNA for

17 putative ribosomal protein portion in said

18 portion of the sample of tumour cells exposed

19 to said chemotherapeutic agent with expression

20 of said one or more genes in a control portion

21 of said sample which has not been exposed to

22 said chemotherapeutic agent; wherein enhanced

23 expression in the portion of sample exposed to

24 said chemotherapeutic agent is indicative of

25 sensitivity to said chemotherapeutic agent.

26

27 3. The method according to claim 2, wherein

28 expression in the portion of sample exposed to

29 said chemotherapeutic agent is considered to

30 be enhanced if the expression is at least 3-

31 fold that of the one or more genes in the

32 control portion of said sample which has not

1 been exposed to said chemotherapeutic agent.

2

3 4. The method according to claim 3, wherein
4 expression in the portion of sample exposed to
5 said chemotherapeutic agent is considered to
6 be enhanced if the expression is at least 10-
7 fold that of the one or more genes in the
8 control portion of said sample which has not
9 been exposed to said chemotherapeutic agent.

10

11 5. The method according to any one of claims 1 to
12 4, wherein said chemotherapeutic agent is a
13 fluoropyrimidine.

14

15 6. The method according to claim 5, wherein said
16 fluoropyrimidine is 5-FU.

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18 7. The method according to any one of claims 1 to
19 4, wherein said chemotherapeutic agent is an
20 antimetabolite.

21

22 8. The method according to claim 7, wherein said
23 antimetabolite is tomudex.

24

25 9. The method according to any one of claims 1 to
26 4, wherein said chemotherapeutic agent is a
27 platinum containing compound.

28

29 10. The method according to claim 9, wherein said
30 platinum containing compound is oxaliplatin.

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1 11. An assay method for identifying a
2 chemotherapeutic agent for use in the treatment
3 of cancer, said method comprising the steps:
4 (a) providing a sample of tumour cells;
5 (b) exposing a portion of said sample to a
6 candidate chemotherapeutic agent;
7 (c) determining expression of one or more of
8 the genes encoding Raf, K-ras, SLAP,
9 phosphoinositide 3-kinase, COP9 homolog
10 (HCOP9), apoptosis specific protein, APO-1 cell
11 surface antigen, FLIP protein, cyclin G, CDC2 ,
12 cyclin-dependent protein kinase -2, thymosin β -
13 10, myosin light chain (MLC-2), gelsolin,
14 thymosin β -4, SSAT, spermidine synthase,
15 spermidine aminopropyltransferase, MAT-8
16 protein, annexin II, annexin IV, FGF receptor
17 2, transmembrane 4 superfamily protein ,
18 chaperonin 10, enoyl-CoA hydratase,
19 nicotinamide nucleotide transhydrogenase,
20 ribosomal protein S28, ribosomal protein L37,
21 and/or ribosomal protein L7 and/or L23 mRNA for
22 putative ribosomal protein in said portion of
23 the sample of tumour cells exposed to said
24 candidate chemotherapeutic agent with
25 expression of said one or more genes in a
26 control portion of said sample which has not
27 been exposed to said candidate chemotherapeutic
28 agent; wherein enhanced expression in the
29 sample exposed to said candidate
30 chemotherapeutic agent compared to expression
31 in the portion of sample not exposed to the
32 candidate chemotherapeutic agent is indicative

1 of chemotherapeutic effect.

2

3 12. The method according to claim 11, wherein
4 expression in the portion of sample exposed to
5 said candidate chemotherapeutic agent is
6 considered to be enhanced if the expression is
7 at least 3-fold that of the one or more genes
8 in the control portion of said sample which has
9 not been exposed to said candidate
10 chemotherapeutic agent.

11

12 13. The method according to claim 12, wherein
13 expression in the portion of sample exposed to
14 said candidate chemotherapeutic agent is
15 considered to be enhanced if the expression is
16 at least 10-fold that of the one or more genes
17 in the control portion of said sample which has
18 not been exposed to said candidate
19 chemotherapeutic agent.

20

21 14. The method according to any one of claims 11
22 to 13, wherein said candidate chemotherapeutic
23 agent is a fluoropyrimidine.

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25 15. The method according to any one of claims 11
26 to 13, wherein said candidate chemotherapeutic
27 agent is an antimetabolite.

28

29 16. The method according to any one of claims 11 to
30 13, wherein said candidate chemotherapeutic
31 agent is a platinum containing compound.

32

- 1 17. A method to predict response of tumour cells to
2 in vivo treatment with 5-FU:
3 (a) providing an in vitro sample containing
4 live tumour cells from a subject;
5 (b) determining the basal expression of one or
6 more of the genes encoding Raf, K-ras, SLAP,
7 phosphoinositide 3-kinase, COP9 homolog
8 (HCOP9), apoptosis specific protein, APO-1 cell
9 surface antigen, FLIP protein, cyclin G, CDC2 ,
10 cyclin-dependent protein kinase -2, thymosin β -
11 10, myosin light chain (MLC-2), gelsolin,
12 thymosin β -4, SSAT, spermidine synthase,
13 spermidine aminopropyltransferase, MAT-8
14 protein, annexin II, annexin IV, FGF receptor
15 2, transmembrane 4 superfamily protein ,
16 chaperonin 10, enoyl-CoA hydratase,
17 nicotinamide nucleotide transhydrogenase,
18 ribosomal protein S28, ribosomal protein L37,
19 and/or ribosomal protein L7 and/or L23 mRNA for
20 putative ribosomal protein in said sample,
21 wherein enhanced basal expression of said one
22 or more of the genes compared to the basal
23 expression level of the corresponding gene(s)
24 in one or more control 5-FU sensitive cancer
25 cell-lines is indicative of 5-FU resistance.
26
- 27 18. The method according to claim 17, wherein the
28 5-FU sensitive cancer cell line is the H630
29 cell line.
30
- 31 19. The method according to any one of claims 1 to
32 18 wherein said one or more genes are one or

1 more of genes encoding Raf, K-ras, SLAP,
2 phosphoinositide 3-kinase, COP9 homolog
3 (HCOP9), apoptosis specific protein, APO-1 cell
4 surface antigen, FLIP protein, cyclin G, CDC2 ,
5 cyclin-dependent protein kinase -2, myosin
6 light chain (MLC-2), gelsolin, thymosin β -4,
7 spermidine synthase, spermidine
8 aminopropyltransferase, annexin IV, FGF
9 receptor 2, transmembrane 4 superfamily
10 protein, enoyl-CoA hydratase, nicotinamide
11 nucleotide transhydrogenase, ribosomal protein
12 S28, ribosomal protein L37, and/or ribosomal
13 protein L7 and/or L23 mRNA for putative
14 ribosomal protein.

15

16 20. The method according to claim 19 wherein said
17 one or more genes are one or more of genes
18 encoding Raf, K-ras, SLAP, phosphoinositide 3-
19 kinase, COP9 homolog (HCOP9), apoptosis
20 specific protein, APO-1 cell surface antigen,
21 FLIP protein, cyclin G, CDC2 , cyclin-dependent
22 protein kinase -2, myosin light chain (MLC-2),
23 gelsolin, thymosin β -4, spermidine synthase,
24 spermidine aminopropyltransferase, FGF receptor
25 2, transmembrane 4 superfamily protein, enoyl-
26 CoA hydratase, nicotinamide nucleotide
27 transhydrogenase, ribosomal protein S28,
28 ribosomal protein L37, and/or ribosomal protein
29 L7 and/or L23 mRNA for putative ribosomal
30 protein.

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1 21. The method according to any one of claims 1 to
2 18 wherein said one or more genes encodes SSAT,
3 annexin II, thymosin- β -10, MAT-8 or Chaperonin-
4 10.

5

6 22. The method according to any one of claims 19 to
7 21, wherein the gene is a gene encoding MAT-8.

8

9 23. The method according to any one of claims 11 to
10 16, wherein said gene is a gene encoding
11 chaperonin-10.

12

13 24. A novel chemotherapeutic agent identified by
14 the method of any one of claims 11 to 16.

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